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Genetic variant of p53 gene linked to breast cancer risk in premenopausal African American women

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Scientists at The Wistar Institute in collaboration with Roswell Park Cancer Institute found a significant association between a rare genetic variant of the p53 gene present in African American women and their risk of developing breast cancer in premenopausal age. The study was published online by the journal *NPJ Breast Cancer*.

TP53 is the most frequently mutated gene in human cancer. The p53 protein is a critical tumor suppressor in the cell and genetic mutations that occur in cancer cause a loss of its function in regulating proliferation arrest and cell death. In addition to these changes, there are several minor, naturally occurring genetic variants of the p53 gene, also known as polymorphisms, and some of them are associated with an increased risk of cancer.

The rare p53 polymorphism analyzed in this study is found almost exclusively in populations of African descent. Wistar scientists have previously shown that this polymorphism impairs the ability of p53 to induce cell death in vitro and significantly increases cancer risk when recreated in a mouse model. The new study analyzed the statistical association of this variant with the risk of developing breast cancer in African American women.

"Based on our previous studies on the functional effects of this genetic variant on the p53 protein, we sought to verify if it alters cancer risk in

human carriers," said Maureen Murphy, Ph.D., professor and program leader of the Molecular and Cellular Oncogenesis Program at Wistar and senior author of the study. "This genetic variant is present exclusively in people of African descent, so our study addresses cancer disparities in African American women, a historically underrepresented group in research studies."

"Our results show that the risk of developing breast cancer is increased by nearly 70 percent in premenopausal women who carry this polymorphism," Murphy said. "Because its frequency is very low in the African American population, larger studies will be needed to confirm our observations."

Murphy and colleagues conducted statistical studies on a cohort of more than 14,000 women of African descent and didn't find any association of the polymorphism with increased breast cancer risk overall. However, as previously observed with other genetic variants of p53, a significant association was present in women in premenopausal age.

Elucidating the effects of p53 polymorphisms on cancer risk is a challenging task, especially due to the limited availability of sample cohorts from specific populations. This study provides a strong suggestion that the genetic variant considered might be associated with a significant increase in breast cancer risk, although this association will need to be confirmed in a larger sample set.

Provided by The Wistar Institute